AMENDMENTS TO THE SPECIFICATION

Please insert the following paragraph as the first paragraph of the Brief Description of Drawings:

The patent or application file contains at least one drawing executed in color. Copies of the patent or patent application publication with color drawing(s) will be provided by the Office upon request and payment of the necessary fee.

Please replace paragraph [11] beginning on page 4 with the following rewritten paragraph:

[11] In one embodiment of the invention, the purine or pyrimidine analog includes a thiol moiety, thereby providing a reactive moiety not normally present in nucleic acids. Other such moieties might include sulfonyl, nitro, chloro, bromo, fluoro, sulfamino, aza, etc. Preferably the analog is not toxic to the cell. The analog may be a pyrimidine analog, e.g. a uracil analog. Analogs of interest include, without limitation, thiouracil, 2,4 dithiouracil, thiol-substituted hypoxanthine, thiol substituted thymidine, and the like. The thiol moiety can readily react with a variety of linkers known in the art, permitting introduction of groups useful in separation and detection, e.g. haptens or molecules having known high affinity ligands, e.g. biotin, digoxigenin, etc.; specific labels, e.g. fluorescein, ~~Cy~~CY3™, ~~Cy~~CY5™, etc.; direct linking to substrate surfaces, e.g. capillaries, magnetic beads, microspheres; and the like.

Please replace paragraph [40] beginning on page 12 and continuing onto page 13 with the following rewritten paragraph:

[40] Viral vectors of interest include, without limitation, retroviral vectors (*e.g.* derived from MoMLV, MSCV, SFFV, MPSV, SNV etc), lentiviral vectors (e.g. derived from HIV-1, HIV-2, SIV, BIV, FIV etc.), adeno- associated virus (AAV) vectors, adenoviral vectors (*e.g.* derived from Ad5 virus), SV40-based vectors, Herpes Simplex Virus (HSV)-based

vectors *etc.* A vector construct may coordinately express the enzyme of interest and a marker gene such that expression of the marker gene can be used as an indicator for the expression of the enzyme of interest, as well as for analysis of gene transfer efficiency. This can be achieved by linking the test and a marker gene with an internal ribosomal entry site (IRES) sequence and expressing both genes from a single bi-cistronic mRNA. IRES sequence could be from a virus (e.g. EMCV, FMDV etc) or a cellular gene (e.g. eIF4G, BiP, Kv1.4 etc). The examples of marker genes include drug resistance genes (neo, dhfr, hprt, gpt, bleo, puro etc) enzymes (ß-galactosidase, alkaline phosphatase, *etc.*) fluorescent genes (*e.g.* GFP, RFP, BFP, YFP) or surface markers (*e.g.* CD24, NGFr, Lyt-2 etc). A preferred marker gene is biologically inactive and can be detected by standard immunological methods. Alternatively, an "epitope tag" could be added to the test gene for detection of protein expression. Examples of such "epitope tags" are c-myc and FLAG™ (Stratagene).

Please replace paragraph [55] beginning on page 16 and continuing onto page 17 with the following rewritten paragraph:

[55] A wide variety of fluorescers can be employed either alone or, alternatively, in conjunction with quencher molecules. Fluorescers of interest fall into a variety of categories having certain primary functionalities. These primary functionalities include 1- and 2-aminonaphthalene, p,p'-diaminostilbenes, pyrenes, quaternary phenanthridine salts, 9-aminoacridines, p,p'-diaminobenzophenone imines, anthracenes. oxacarbocyanine, marocyanine, 3-aminoequilenin, perylene, bisbenzoxazole, bis-p-oxazolyl benzene, 1,2-benzophenazin, retinol, bis-3-aminopyridinium salts, hellebrigenin, tetracycline, sterophenol, benzimidzaolylphenylamine, 2-oxo-3 -chromen, indole, xanthen, 7-hydroxycoumarin, phenoxazine, salicylate, strophanthidin, porphyrins, triarylmethanes and flavin. Individual fluorescent compounds which have functionalities for linking or which can be modified to incorporate such functionalities include, *e.g.*, dansyl chloride; fluoresceins

such as 3,6-dihydroxy-9-phenylxanthhydrol; rhodamineisothiocyanate; N-phenyl 1-amino-8-sulfonatonaphthalene; N-phenyl 2-amino-6-sulfonatonaphthalene: 4-acetamido-4-isothiocyanato-stilbene-2,2'-disulfonic acid; pyrene-3-sulfonic acid; 2-toluidinonaphthalene-6-sulfonate; N-phenyl, N-methyl 2-aminoaphthalene-6-sulfonate; ethidium bromide; stebrine; auromine-0,2-(9'-anthroyl)palmitate; dansyl phosphatidylethanolamine; N,N'-dioctadecyl oxacarbocyanine; N,N'-dihexyl oxacarbocyanine; merocyanine, 4(3'pyrenyl)butyrate; d-3-aminodesoxy-equilenin; 12-(9'anthroyl)stearate; 2-methylanthracene; 9-vinylanthracene; 2,2'(vinylene-p-phenylene)bisbenzoxazole; p-bis[2-(4-methyl-5-phenyl-oxazolyl)]benzene; 6-dimethylamino-1,2-benzophenazin; retinol; bis(3'-aminopyridinium) 1,10-decandiyl diiodide; sulfonaphthylhydrazone of hellibrienin; chlorotetracycline; N(7-dimethylamino-4-methyl-2-oxo-3-chromenyl)maleimide; N-[p-(2-benzimidazolyl)-phenyl]maleimide; N-(4-fluoranthyl)maleimide; bis(homovanillic acid); resazarin; 4-chloro-7-nitro-2,1,3benzooxadiazole; merocyanine 540; resorufin; rose bengal; and 2,4-diphenyl-3(2H)-furanone. Specific fluorochromes of interest include fluorescein isothiocyanate (FITC™), rhodamine, ~~Texas Red~~ **TEXAS RED** ™, phycoerythrin, allophycocyanin, 6-carboxyfluorescein (6-FAM™), 2',7'-dimethoxy-4',5'-dichloro-6-carboxyfluorescein (JOE™), 6-carboxy-X-rhodamine (ROX™), 6-carboxy-2',4',7',4,7-hexachlorofluorescein (HEX™), 5-carboxyfluorescein (5-FAM™) or N,N,N',N'-tetramethyl-6-carboxyrhodamine (TAMRA™). Cyanine dyes are of particular interest as a detectable label. Cyanine dyes are synthetic dyes in which a nitrogen and part of a conjugated chain form part of a heterocyclic system, such as imidazole, pyridine, pyrrole, quinoline and thiazoles; including ~~Cy~~**CY**3™ and ~~Cy~~**CY**5™, which are widely used as labels. Such directly labeled RNA can be used in hybridization analysis without further manipulation.

Please replace paragraph [58] beginning on page 18 with the following rewritten paragraph:

[58] Biotinylated RNA can be separated by affinity chromatography with a biotin binding partner, e.g. avidin, streptavidin, neutravidin; etc.; or can combined with a labeled biotin binding partner, e.g. ~~Cy~~CY5™ -avidin; ~~Cy~~CY3™ -avidin; and for purposes of, for example, in situ hybridization, can be combined with a radiolabeled or heavy metal labeled binding partner.

Please replace paragraph [86] beginning on page 26 with the following rewritten paragraph:

[86] Having shown that the Toxoplasma ribosomal RNA could be specifically labeled and purified, we next asked if the parasite's mRNA could also be purified and whether this mRNA could be used in microarray experiments. To do this, we used the thiouracil-labeled RNA that had been specifically eluted from the streptavidin beads as a substrate for reverse transcriptase (i.e., cDNA synthesis) in the presence of ~~cy~~CY5™-labeled nucleotides. This material was used in microarray experiments and compared to results from a separate microarray in which RNA from parasites grown in the absence of 2,4-dithiouracil was made into cDNA in the presence of ~~cy~~CY5™ labeled nucleotides.

Please replace paragraph [87] beginning on page 26 with the following rewritten paragraph:

[87] Methods and Results: The two RNAs were compared for their ability to bind to spotted cDNA probes corresponding to Toxoplasma genes in a microarray as previously described. 2 µg of RNA from both samples was labeled with cy5™ during first strand cDNA synthesis and each cy5™ labeled sample was mixed with a common cy3™ reference probe and hybridized to separate microarrays. The data (FIG. 3) showed that the thiouracil-labeled mRNA served well as a template for the cDNA synthesis and that the hybridization was globally similar to that seen with unlabeled mRNA, as expected since the incorporation of thiouracil was

over a 40 hour period and thus would be expected to completely saturate all mRNAs.

Please replace paragraph [90] beginning on page 27 with the following rewritten paragraph:

[90] Methods and Results: To compare results obtained by measurement of mRNA abundance versus measurement of mRNA synthesis, microarray analysis was performed using either total mRNA or purified thiouracil RNA following a one hour pulse. Total and pulse-labeled mRNAs were prepared from parasites grown in human foreskin fibroblast cultures maintained in either neutral pH media or high pH media. Growth in high pH induces parasites to develop into a developmental stage known as a bradyzoite while parasites grown in neutral pH grow as a distinct stage known as a tachyzoite. Following four hours of growth as tachyzoites, cultures of parasites were either kept in neutral pH media for 48 hrs or switched to high pH media for 72 hours. Comparison of gene expression between tachyzoites and bradyzoites at these timepoints has been published, using traditional microarray techniques (i.e. mRNA abundance measurements). At the end of each timepoint, 48 or 72 hours, the media was removed and media containing 2 mM 2,4-dithiouracil (at the corresponding pH) was added for one hour. At the end of this hour, RNA was prepared using Trizol and mRNA was purified using the FastTrak mRNA isolation kit from Invitrogen. An aliquot from each mRNA sample was used in microarray analysis of total mRNA abundance. The remaining mRNA was biotinylated and purified over streptavidin magnetic beads as described above. This RNA was used in microarray experiments to measure the mRNA synthesized during the one hour 2,4-dithiouracil pulse. In all microarray experiments, 150 ng of Toxoplasma mRNA was labeled with ~~cy~~CY5™ dUTP and compared to a common ~~cy~~CY3™ labeled reference sample. The ratio of mRNA in bradyzoites and tachyzoites was determined for both the total abundance

and the pulse-labeled mRNA microarrays, using previously described analysis methods.